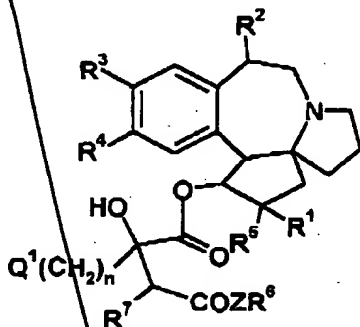


THERAPEUTICAL METHOD INVOLVING SUBCUTANEOUS ADMINISTRATION OF DRUGS CONTAINING CEPHALOTAXINE DERIVATIVES

ABSTRACT

A new method of therapy using the subcutaneous mode of administration of formulations based upon harringtonines including their salts and tautomeric forms having the formula



where :

R^1 is H, OH, OMe, O-(C₁-C₃₀)-alkyl, O-aryl-(C₁-C₃₀)-alkyl, O-(C₂-C₃₀)-alkenyl, O-(C₃-C₃₀)-cycloalkyl or null and

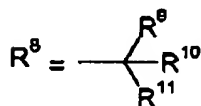
R^2 is H or OH, or R^1 , R^2 form together -O-.

$R^3 = R^4 = \text{OMe}$ or R^3 and R^4 form together -OCH₂O-,

n is 0 to 8,

R^5 is H, OH, OMe, O-(C₁-C₃₀)-alkyl, O-aryl-(C₁-C₃₀)-alkyl, O-(C₂-C₃₀)-alkenyl, O-(C₃-C₃₀)-cycloalkyl or O-aryl,

$Z = \text{O}, \text{S}, \text{or NH}$, and



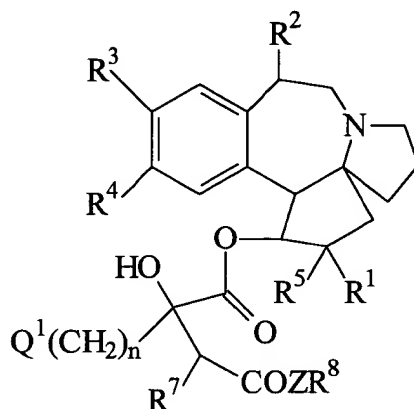
or $Z-R^6$ is $\text{NR}^{12}\text{R}^{13}$, R^{12} and R^{13} representing respectively R^8 and R^{10} ,

$$\text{---}(\text{CH}_2)_m\text{---}\begin{array}{c} \text{R}^{14} \quad \text{R}^{15} \\ \diagdown \quad \diagup \\ \text{C}=\text{C} \\ \diagup \quad \diagdown \\ \text{R}^{16} \end{array}$$

or their combination with another antitumor agent or a mixture of antitumor agents useful for the treatment of a disease in humans or animals, particularly cancers, leukemias, lymphomas, parasite diseases or chemotherapeutic resistance to other agents, in using a formulation specifically adapted for subcutaneous administration.

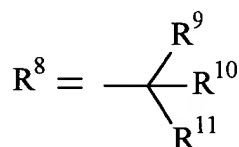
--ABSTRACT

A new method of therapy using the subcutaneous mode of administration of formulations based upon harringtonines including their salts and tautomeric forms having the formula:



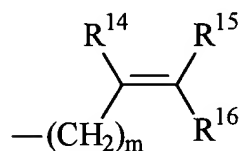
wherein:

- R^1 is H, OH, OMe, O-(C₁-C₃₀)-alkyl, O-aryl-(C₁-C₃₀)-alkyl, O-(C₂-C₃₀)-alkenyl, O-(C₃-C₃₀)-cycloalkyl or null and
 R^2 is H or OH, or R^1 , R^2 form together -O-,
 $R^3 = R^4 =$ OMe or R^3 and R^4 form together -OCH₂O-,
- n is 0 to 8,
- R^5 is H, OH, OMe, O-(C₁-C₃₀)-alkyl, O-aryl-(C₁-C₃₀)-alkyl, O-(C₂-C₃₀)-alkenyl, O-(C₃-C₃₀)-cycloalkyl or O-aryl,
Z = O, S, or NH, and



or Z-R⁸ is NR¹²R¹³, R¹² and R¹³ representing respectively R⁹ and R¹⁰,

R^9 , R^{10} , R^{11} are independently H, C_1 - C_{30} alkyl, C_3 - C_{30} cycloalkyl, aryl, aryl-(C_1 - C_{30})-alkyl, C_2 - C_{30} alkenyl, C_2 - C_{30} alkynyl, C_1 - C_{30} trihalogenoalkyl, C_1 - C_{30} alkylamino-(C_1 - C_{30})alkyl, C_1 - C_{30} dialkylamino(C_1 - C_{30})-alkyl, or amino-(C_1 - C_{30})-alkyl, or



where R^{14} , R^{15} , R^{16} are independently H, halogen, C_1 - C_{30} alkyl, C_3 - C_{30} cycloalkyl, aryl, aryl-(C_1 - C_{30})-alkyl, C_2 - C_{30} alkenyl or C_2 - C_{30} alkynyl, or C_1 - C_{30} trihalogenoalkyl, and m is 0 to 4,

each of these groups including or not heteroatom(s),
or salt or tautomeric form thereof.--